



SEQUENCE LISTING

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<120> Gene-Mutated Animal

<130> P19743

<140> 09/581,528

<141> 2000-10-26

<150> PCT/JP99/00015

<151> 1999-01-07

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<151> 1998-01-08

<160> 22

<170> PatentIn version 3.3

<210> 1

<211> 467

<212> PRT

<213> Human

<400> 1

Met Thr Glu Leu Pro Ala Asx Leu Ser Tyr Phe Gln Asn Ala Gln Met
1 5 10 15

Ser Glu Asp Asn His Leu Ser Asn Thr Val Arg Ser Gln Asn Asp Asn
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Arg Glu Arg Gln Glu His Asn Asp Arg Arg Ser Leu Gly His Pro Glu
35 40 45

Pro Leu Ser Asn Gly Arg Pro Gln Gly Asn Ser Arg Gln Val Val Glu
50 55 60

Gln Asp Glu Glu Glu Asp Glu Glu Leu Thr Leu Lys Tyr Gly Ala Lys
65 70 75 80

His Val Ile Met Leu Phe Val Pro Val Thr Leu Cys Met Val Val Val
 85 90 95

Val Ala Thr Ile Lys Ser Val Ser Phe Tyr Thr Arg Lys Asp Gly Gln
 100 105 110

Leu Ile Tyr Thr Pro Phe Thr Glu Asp Thr Glu Thr Val Gly Gln Arg
 115 120 125

Ala Leu His Ser Ile Leu Asn Ala Ala Ile Met Ile Ser Val Ile Val
 130 135 140

Val Met Thr Ile Leu Leu Val Val Leu Tyr Lys Tyr Arg Cys Tyr Lys
 145 150 155 160

Val Ile His Ala Trp Leu Ile Ile Ser Ser Leu Leu Leu Leu Phe Phe
 165 170 175

Phe Ser Phe Ile Tyr Leu Gly Glu Val Phe Lys Thr Tyr Asn Val Ala
 180 185 190

Val Asp Tyr Ile Thr Val Ala Leu Leu Ile Trp Asn Phe Gly Val Val
 195 200 205

Gly Met Ile Ser Ile His Trp Lys Gly Pro Leu Arg Leu Gln Gln Ala
 210 215 220

Tyr Leu Ile Met Ile Ser Ala Leu Met Ala Leu Val Phe Ile Lys Tyr
 225 230 235 240

Leu Pro Glu Trp Thr Ala Trp Leu Ile Leu Ala Val Ile Ser Val Tyr
 245 250 255

Asp Leu Asp Ala Val Leu Cys Pro Lys Gly Pro Leu Arg Met Leu Val
 260 265 270

Glu Thr Ala Gln Glu Arg Asn Glu Thr Leu Phe Pro Ala Leu Ile Tyr
 275 280 285

Ser Ser Thr Met Val Trp Leu Val Asn Met Ala Glu Gly Asp Pro Glu
 290 295 300

Ala Gln Arg Arg Val Ser Lys Asn Ser Lys Tyr Asn Ala Glu Ser Thr
 305 310 315 320

Glu Arg Glu Ser Gln Asp Thr Val Ala Glu Asn Asp Asp Gly Gly Phe
 325 330 335

Ser Glu Glu Trp Glu Ala Gln Arg Asp Ser His Leu Gly Pro His Arg
 340 345 350

Ser Thr Pro Glu Ser Arg Ala Ala Val Gln Glu Leu Ser Ser Ser Ile
 355 360 365

Leu Ala Gly Glu Asp Pro Glu Glu Arg Gly Val Lys Leu Gly Leu Gly
 370 375 380

Asp Phe Ile Phe Tyr Ser Val Leu Val Gly Lys Ala Ser Ala Thr Ala
 385 390 395 400

Ser Gly Asp Trp Asn Thr Thr Ile Ala Cys Phe Val Ala Ile Leu Ile
 405 410 415

Gly Leu Cys Leu Thr Leu Leu Leu Leu Ala Ile Phe Lys Lys Ala Leu
 420 425 430

Pro Ala Leu Pro Ile Ser Ile Thr Phe Gly Leu Val Phe Tyr Phe Ala
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Thr Asp Tyr Leu Val Gln Pro Phe Met Asp Gln Leu Ala Phe His Gln
 450 455 460

Phe Tyr Ile
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<212> DNA
<213> Human

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120

agacggagcc ttggccaccc tgagccatta tctaattggac gaccccaggg taactcccgg
180

caggtggtgg agcaagatga ggaagaagat gaggagctga cattgaaata tggcgccaag
240

catgtgatca tgctctttgt ccctgtgact ctctgcatgg tggtggtcgt ggctactatt
300

aagtcagtca gcttttatac ccggaaggat gggcagctaa tctatacccc attcacagaa
360

gataccgaga ctgtgggcca gagagccctg cactcaattc tgaatgctgc catcatgac
420

agtgtcattg ttgtcatgac taccctcctg gtggttctgt ataaatacag gtgctataag
480

gtcatccatg cctggcttat tatatcatct ctattgttgc tgttcttttt ttcattcatt
540

tacttggggg aagtgtttaa aacctataac gttgctgtgg actacattac tgttgcactc
600

ctgatctgga attttggtgt ggtgggaatg atttccattc actggaaagg tccacttcga
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ctccagcagg catatctcat tatgattagt gccctcatgg ccctgggtgtt tatcaagtac
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780

gttttggtgc cgaaaggtcc acttcgtatg ctggttgaaa cagctcagga gagaaatgaa
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acgctttttc cagctctcat ttactcctca acaatgggtg gggttggtgaa tatggcagaa
900

ggagacccgg aagctcaaag gagagtatcc aaaaattcca agtataatgc agaaagcaca
960

gaaagggagt cacaagacac tgttgcagag aatgatgatg gcggggttcag tgaggaatgg
1020

gaagcccaga gggacagtca tctagggcct catcgctcta cacctgagtc acgagctgct
1080

gtccaggaac tttccagcag tatcctcgct ggtgaagacc cagaggaaag gggagtaaaa
1140

cttggtattg gagatttcat tttctacagt gttctgggtg gtaaagcctc agcaacagcc
1200

agtggagact ggaacacaac catagcctgt ttcgtagcca tattaattgg tttgtgcctt
1260

acattattac tccttgccat tttcaagaaa gcattgccag ctcttccaat ctccatcacc
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<210> 3
<211> 467
<212> PRT
<213> Mouse

<400> 3

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Ser Glu Asp Ser His Ser Ser Ser Ala Ile Arg Ser Gln Asn Asp Ser

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Glu	Glu	Arg	Gln	Gln	Gln	His	Asp	Arg	Gln	Arg	Leu	Asp	Asn	Pro	Glu
		35					40					45			
Pro	Ile	Ser	Asn	Gly	Arg	Pro	Gln	Ser	Asn	Ser	Arg	Gln	Val	Val	Glu
	50					55					60				
Gln	Asp	Glu	Glu	Glu	Asp	Glu	Glu	Leu	Thr	Leu	Lys	Tyr	Gly	Ala	Lys
65					70					75					80
His	Val	Ile	Met	Leu	Phe	Val	Pro	Val	Thr	Leu	Cys	Met	Val	Val	Val
				85					90					95	
Val	Ala	Thr	Ile	Lys	Ser	Val	Ser	Phe	Tyr	Thr	Arg	Lys	Asp	Gly	Gln
			100					105					110		
Leu	Ile	Tyr	Thr	Pro	Phe	Thr	Glu	Asp	Thr	Glu	Thr	Val	Gly	Gln	Arg
		115					120					125			
Ala	Leu	His	Ser	Ile	Leu	Asn	Ala	Ala	Ile	Met	Ile	Ser	Val	Ile	Val
	130					135					140				
Ile	Met	Thr	Ile	Leu	Leu	Val	Val	Leu	Tyr	Lys	Tyr	Arg	Cys	Tyr	Lys
145				150						155					160
Val	Ile	His	Ala	Trp	Leu	Ile	Ile	Ser	Ser	Leu	Leu	Leu	Leu	Phe	Phe
				165					170					175	
Phe	Ser	Phe	Ile	Tyr	Leu	Gly	Glu	Val	Phe	Lys	Thr	Tyr	Asn	Val	Ala
			180					185					190		
Val	Asp	Tyr	Val	Thr	Val	Ala	Leu	Leu	Ile	Trp	Asn	Phe	Gly	Val	Val
	195						200					205			
Gly	Met	Ile	Ala	Ile	His	Trp	Lys	Gly	Pro	Leu	Arg	Leu	Gln	Gln	Ala

210					215					220					
Tyr	Leu	Ile	Met	Ile	Ser	Ala	Leu	Met	Ala	Leu	Val	Phe	Ile	Lys	Tyr
225					230					235					240
Leu	Pro	Glu	Trp	Thr	Ala	Trp	Leu	Ile	Leu	Ala	Val	Ile	Ser	Val	Tyr
				245					250					255	
Asp	Leu	Val	Ala	Val	Leu	Cys	Pro	Lys	Gly	Pro	Leu	Arg	Met	Leu	Val
			260					265					270		
Glu	Thr	Ala	Gln	Glu	Arg	Asn	Glu	Thr	Leu	Phe	Pro	Ala	Leu	Ile	Tyr
		275					280					285			
Ser	Ser	Thr	Met	Val	Trp	Leu	Val	Asn	Met	Ala	Glu	Gly	Asp	Pro	Glu
	290					295					300				
Ala	Glu	Arg	Arg	Val	Pro	Lys	Asn	Pro	Lys	Tyr	Asn	Thr	Gln	Arg	Ala
305					310					315					320
Glu	Arg	Glu	Thr	Gln	Asp	Ser	Gly	Ser	Gly	Asn	Asp	Asp	Gly	Gly	Phe
				325					330					335	
Ser	Glu	Glu	Trp	Glu	Ala	Gln	Arg	Asp	Ser	His	Leu	Gly	Pro	His	Arg
			340					345					350		
Ser	Thr	Pro	Glu	Ser	Arg	Ala	Ala	Val	Gln	Glu	Leu	Ser	Gly	Ser	Ile
		355					360					365			
Leu	Thr	Ser	Glu	Asp	Pro	Glu	Glu	Arg	Gly	Val	Lys	Leu	Gly	Leu	Gly
	370					375					380				
Asp	Phe	Ile	Phe	Tyr	Ser	Val	Leu	Val	Gly	Lys	Ala	Ser	Ala	Thr	Ala
385					390					395					400
Ser	Gly	Asp	Trp	Asn	Thr	Thr	Ile	Ala	Cys	Phe	Val	Ala	Ile	Leu	Ile

405

410

415

Gly Leu Cys Leu Thr Leu Leu Leu Leu Ala Ile Phe Lys Lys Ala Leu
 420 425 430

Pro Ala Leu Pro Ile Ser Ile Thr Phe Gly Leu Val Phe Tyr Phe Ala
 435 440 445

Thr Asp Tyr Leu Val Gln Pro Phe Met Asp Gln Leu Ala Phe His Gln
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Phe Tyr Ile
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 <212> DNA
 <213> Mouse

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 120

aggcagagac ttgacaaccc tgagccaata tctaattgggc ggccccagag taactcaaga
 180

caggtggtgg aacaagatga ggaggaagac gaagagctga cattgaaata tggagccaag
 240

catgtcatca tgctctttgt ccccgtagacc ctctgcatgg tcgtcgtcgt ggccaccatc
 300

aatcagtcg gcttctatac ccggaaggac ggtcagctaa tctacacccc attcacagaa
 360

gacactgaga ctgtaggcca aagagccctg cactcgatcc tgaatgcggc catcatgatc
 420

agtgtcattg tcattatgac catcctcctg gtggtcctgt ataaatacag gtgctacaag
 480

gtcatccacg cctggcttat tatttcacat ctgttggtgc tgttcttttt ttcgttcatt
540

tacttagggg aagtatttaa gacctacaat gtcgccgtgg actacgttac agtagcactc
600

ctaactctgga attttggtgt ggtcgggatg attgccatcc actggaaagg ccccttcga
660

ctgcagcagg cgtatctcat tatgatcagt gccctcatgg ccctgggtatt tatcaagtac
720

ctccccgaat ggaccgcatg gctcatcttg gctgtgattt cagtatatga tttggtggct
780

gttttatgtc ccaaaggccc acttcgtatg ctggttgaaa cagctcagga aagaaatgag
840

actctctttc cagctcttat ctattcctca acaatgggtg ggttggtgaa tatggctgaa
900

ggagaccag aagcccaaag gaggtaccc aagaacccca agtataacac acaaagagcg
960

gagagagaga cacaggacag tggttctggg aacgatgatg gtggcttcag tgaggagtgg
1020

gaggcccaa gagacagtca cctggggcct catcgctcca ctcccagtc aagagctgct
1080

gtccaggaac tttctgggag cattctaacg agtgaagacc cggaggaaag aggagtaaaa
1140

cttgactgg gagatttcat tttctacagt gttctggttg gtaaggcctc agcaaccgcc
1200

agtggagact ggaacacaac catagcctgc tttgtagcca tactgatcgg cctgtgcctt
1260

acattactcc tgctcgccat tttcaagaaa gcgttgccag cctccccat ctccatcacc
1320

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1380

gcattccatc agttttatat ctag
1404

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<220>
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<210> 6
 <211> 23
 <212> DNA
 <213> Artificial

<220>
 <223> Primer

<400> 6
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 23

<210> 7
 <211> 36
 <212> DNA
 <213> Artificial

<220>
 <223> Primer

<400> 7
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 36

<210> 8
 <211> 36
 <212> DNA
 <213> Artificial

<220>
 <223> Primer

<400> 8
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36

<210> 9
<211> 18
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 9
tctagacggc cgtctaga
18

<210> 10
<211> 18
<212> DNA
<213> Artificial

<220>
<223> Primer

<400> 10
agatctgccg gcagatct
18

<210> 11
<211> 30
<212> DNA
<213> Artificial

<220>
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<400> 11
cccaactcta tttctaccct cgttcatctg
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<210> 12
<211> 30
<212> DNA

<213> Artificial

<220>

<223> Primer

<400> 12

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30

<210> 13

<211> 30

<212> DNA

<213> Artificial

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<223> Primer

<400> 13

tgctggagga aaatgtgtta tttaagagca
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<210> 14

<211> 30

<212> DNA

<213> Artificial

<220>

<223> Primer

<400> 14

tactgaaatc acagccaaga tgagccatgc
30

<210> 15

<211> 30

<212> DNA

<213> Artificial

<220>

<223> Primer

<400> 15

ggtccatccc agcttcacac agacaagtct
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<210> 16
 <211> 30
 <212> DNA
 <213> Artificial

<220>
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<400> 16
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 30

<210> 17
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 <212> DNA
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<220>
 <223> Primer

<400> 17
 tagtgagacg tgctacttcc atttgtcacg
 30

<210> 18
 <211> 36
 <212> DNA
 <213> Artificial

<220>
 <223> synthetic construct

<220>
 <221> misc_feature
 <222> (16)..(16)
 <223> y is t or c

<220>
 <221> misc_feature
 <222> (20)..(22)
 <223> wherein v is a base other than t; and wherein avc represents
 a
 codon, as triplet bases of a mutant presenilin-1 gene, encod
 ing

an amino acid.

<400> 18
tgtgggtcggg atgatygccca vccactggaa aggccc
36

<210> 19
<211> 36
<212> DNA
<213> Artificial

<220>
<223> synthetic construct

<220>
<221> misc_feature
<222> (16)..(16)
<223> y is t or c

<220>
<221> misc_feature
<222> (20)..(22)
<223> wherein acc represents a codon, as triplet bases of a mutant
presenilin-1 gene, encoding an amino acid.

<400> 19
tgtgggtcggg atgatygccca cccactggaa aggccc
36

<210> 20
<211> 36
<212> DNA
<213> Artificial

<220>
<223> synthetic construct

<220>
<221> misc_feature
<222> (16)..(16)
<223> y is t or c

<220>

<221> misc_feature
 <222> (20)..(22)
 <223> wherein each n is independently chosen from any base; and nn
 n
 1 represents a codon, as triplet bases of a mutant presenilin-
 gene, encoding an amino acid other than isoleucine.

<400> 20
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 36

<210> 21
 <211> 12
 <212> DNA
 <213> Artificial

<220>
 <223> oligodeoxynucleotide targeting vector

<400> 21
 ctagacggcc gt
 12

<210> 22
 <211> 18
 <212> DNA
 <213> Artificial

<220>
 <223> vector

<400> 22
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 18